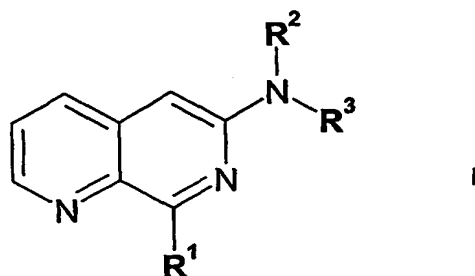


CLAIMS

1. A compound of formula I



in free or salt form, where

R¹ is a monovalent aromatic group having up to 10 carbon atoms, and

R² and R³ together with the nitrogen atom to which they are attached denote a heterocyclic group having up to 10 ring atoms and having 1 to 4 hetero atoms in the ring system.

2. A compound according to claim 1, in which

R¹ is phenyl substituted by one or two substituents selected from cyano, halogen, carboxy or C₁-C₄-haloalkoxy, and optionally by C₁-C₄-alkyl or C₁-C₄-alkoxy, or R¹ is phenyl substituted by C₁-C₄-alkoxy, and

R² and R³ together with the nitrogen atom to which they are attached denote a heterocyclic group having up to 6 ring atoms and one or two hetero atoms in the ring.

3. A compound according to claim 1, in which

R¹ is phenyl substituted by one or two substituents selected from cyano, halogen, carboxy or C₁-C₄-haloalkoxy meta to the indicated naphthyridine ring and optionally by C₁-C₄-alkyl or C₁-C₄-alkoxy ortho to the indicated naphthyridine ring, or R¹ is phenyl substituted by C₁-C₄-alkoxy meta to the indicated naphthyridine ring, and

R² and R³ together with the nitrogen atom to which they are attached denote a heterocyclyl group having up to 6 ring atoms and one or two nitrogen atoms, or one nitrogen atom and one oxygen atom, in the ring, optionally substituted by hydroxy, carboxy, 5-membered O-heterocyclylcarbonyl, aminocarbonyl, C₁-C₄-alkoxycarbonyl, C₁-C₄-alkylsulfonyl or C₁-C₄-alkyl optionally substituted by hydroxy, cyano, carboxy or C₁-C₄-alkoxycarbonyl.

4. A compound according to claim 1 in which

R¹ is phenyl optionally substituted by one, two or three substituents selected from the group consisting of cyano, C₁-C₈-alkyl, C₁-C₈-alkylthio, -SO-C₁-C₈-alkyl, and phenyl fused with a heterocyclic ring having 3 to 8 ring atoms of which up to 4 can be carbon atoms and up to 4 can be hetero atoms, and

R² and R³ together with the nitrogen atom to which they are attached denote a heterocyclic group having up to 6 ring atoms and one or two hetero atoms in the ring optionally substituted by carboxy, carboxy-C₁-C₈-alkoxy or C₁-C₈-alkoxycarbonyl-C₁-C₈-alkoxy, said heterocyclic group also optionally being substituted by C₁-C₈-alkyl or C₁-C₈-alkoxy.

5. A compound according to claim 4, in which

R¹ is phenyl optionally substituted by one, two or three substituents selected from the group consisting of cyano, C₁-C₄-alkyl, C₁-C₄-alkylthio, -SO-C₁-C₄-alkyl, and phenyl fused with a heterocyclic ring having 5 or 6 ring atoms of which up to 4 can be carbon atoms and up to 2 can be hetero atoms, and

R² and R³ together with the nitrogen atom to which they are attached denote a heterocyclic group having up to 6 ring atoms and one or two nitrogen atoms in the ring optionally substituted by carboxy, carboxy-C₁-C₄-alkoxy or C₁-C₄-alkoxycarbonyl-C₁-C₄-alkoxy, said heterocyclic group also optionally being substituted by C₁-C₄-alkyl.

6. A compound according to claim 1, which is

3-[6-(3-hydroxy-pyrrolidin-1-yl)-[1,7]naphthyridin-8-yl]-benzonitrile;

3-[6-[4-(2-cyano-ethyl)-piperazin-1-yl]-[1,7]naphthyridin-8-yl]-benzonitrile;

1-[8-(3-cyano-phenyl)-[1,7]naphthyridin-6-yl]-piperidine-4-carboxylic acid, lithium salt; or

3-(6-piperazin-1-yl-[1,7]naphthyridin-8-yl)-benzonitrile;

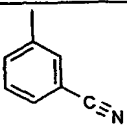
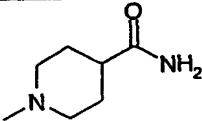
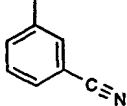
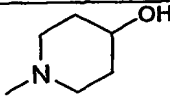
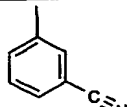
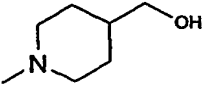
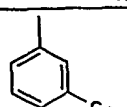
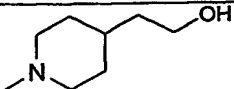
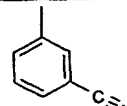
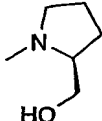
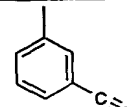
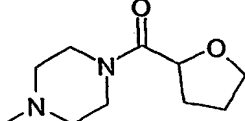
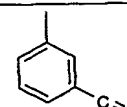
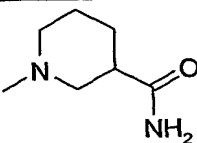
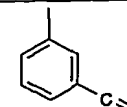
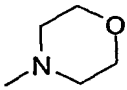
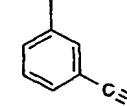
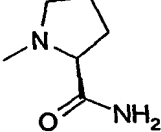
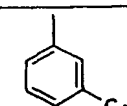
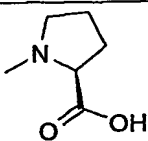
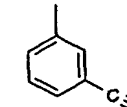
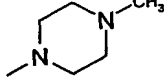
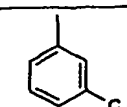
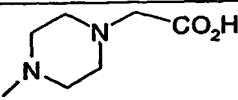
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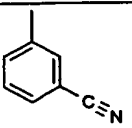
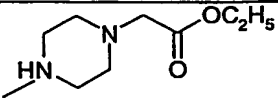
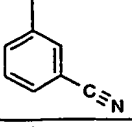
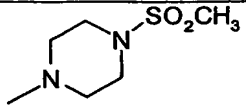
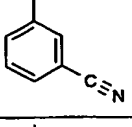
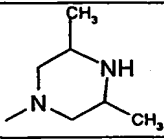
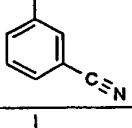
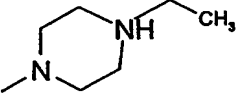
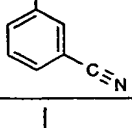
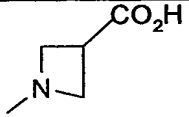
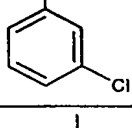
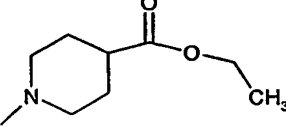
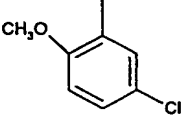
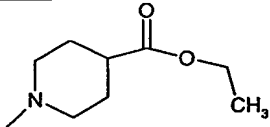
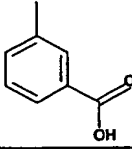
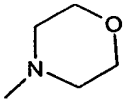
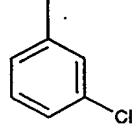
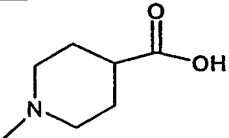
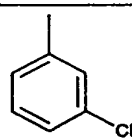
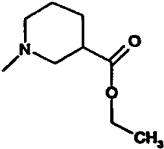
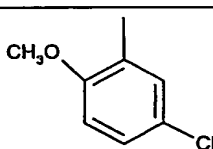
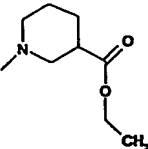
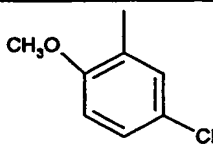
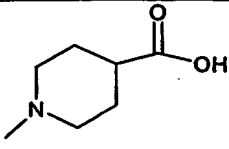
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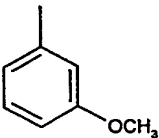
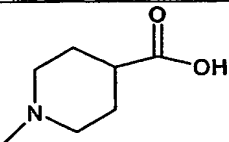
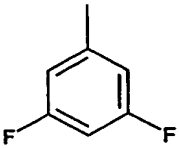
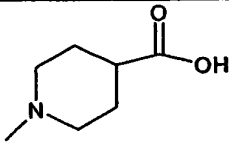
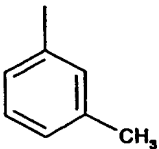
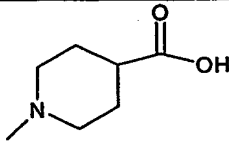
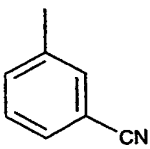
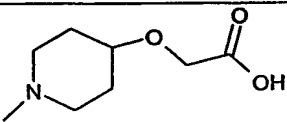
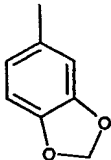
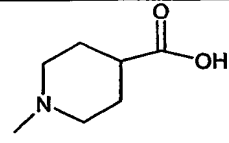
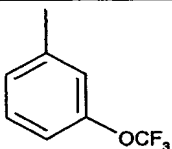
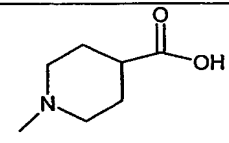
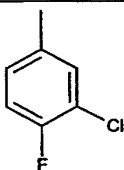
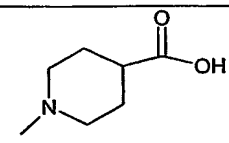
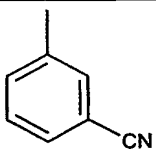
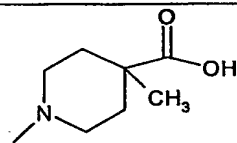
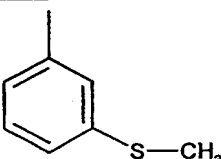
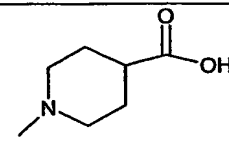
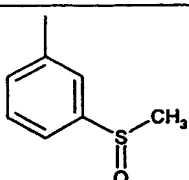
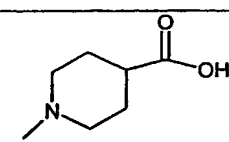
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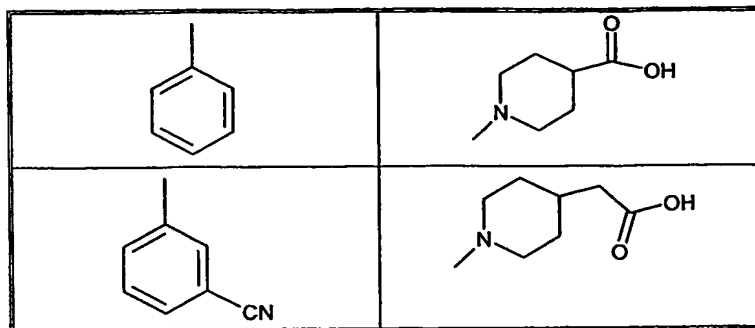
potassium 1-[8-(5-fluoro-2-methoxy-phenyl)-[1,7]naphthyridin-6-yl]-piperidine-4-carboxylate.

7. A compound according to claim 1, wherein R¹ and -NR²R³ are as shown in the following table:

R^1	NR^2R^3
	
	
	
	
	
	
	
	
	
	
	
	

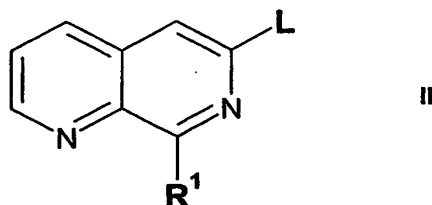
	
	
	
	
	
	
	
	
	
	
	
	

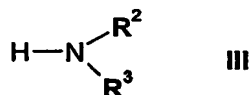


8. A compound according to any one of the preceding claims for use as a pharmaceutical.
9. A pharmaceutical composition comprising a compound according to any one of claims 1 to 7, optionally together with a pharmaceutically acceptable diluent or carrier.
9. Use of a compound according to any one of claims 1 to 7 for the preparation of a medicament for the treatment of a condition mediated by PDE4.
10. Use of a compound according to any one of claims 1 to 7 for the preparation of a medicament for the down-regulation or inhibition of TNF- α release.
11. Use of a compound according to any one of claims 1 to 7 for the preparation of a medicament for the treatment of an inflammatory disease.
12. Use of a compound according to any one of claims 1 to 7 for the preparation of a medicament for the treatment of an obstructive or inflammatory airways disease.
13. A process for the preparation of compounds of formula I in free or salt form which comprises

(iii) (A) reacting a compound of formula



optionally in protected form, where R^1 is as hereinbefore defined and L is a leaving atom or group, for example halogen or an aliphatic or aromatic sulfonyloxy group such as trifluoromethylsulfonyloxy, with a compound of formula



optionally in protected form, where R^2 and R^3 are as hereinbefore defined, followed by deprotection if required;

(B) reacting a compound of formula I, where R^2 and R^3 together with the attached nitrogen atom denote a heterocyclyl group substituted by a C_1 - C_8 -alkoxycarbonyl group, to convert the alkoxycarbonyl group into a carboxy;

(C) for the preparation of compounds of formula I where R^2 and R^3 together with the attached nitrogen atom denote a heterocyclyl group substituted by carboxy- C_1 - C_8 -alkoxy, hydrolysing a compound of formula I where R^2 and R^3 together with the attached nitrogen atom denote a heterocyclyl group substituted by C_1 - C_8 -alkoxycarbonyl- C_1 - C_8 -alkoxy; or

(D) for the preparation of compounds of formula I when R^1 is phenyl substituted by -SO- C_1 - C_8 -alkyl, oxidising a compound of formula I where R^1 is phenyl substituted by C_1 - C_8 -alkylthio; and

(iv) recovering the product in free or salt form.